Cross-Species Mode of Action Information Assessment for Bisphenol A

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Key Words: mode of action, endocrine disrupting chemicals, integrated risk assessment, cross-species extrapolation

An approach to using mode of action (MOA) information across species was developed to support integrated ecological and human health assessment. By assessing the MOA and effects data for a given toxic agent, the relationship between MOA and species relatedness (i.e., evolutionary relationships) could be determined. A case study assessing the utility of the approach was performed for Bisphenol A (BPA). BPA is a component of polycarbonate plastics, epoxy resins, and polyester resins. BPA was selected because it is a high production volume chemical, there are data for some mammalian, nonmammalian, and invertebrate species, and the estrogen agonist MOA (i.e., binding and activating the estrogen receptor to transcribe estrogen-responsive genes) has been fairly well described for a number of vertebrate species.

Cross-species MOA information for developmental and reproductive effects of BPA limited to the animal kingdom was gathered from the literature and the relationship between species relatedness and MOA was assessed. MOA was defined as the key step in the toxic response after chemical interaction at the target site that is responsible for the physiological outcome or pathology. Reproductive and/or developmental in vivo effects data for BPA were identified for 17 species representing 7 animal classes (gastropods, crustaceans, insects, amphibians, fish, birds, and mammals) in 3 phyla. For the tested invertebrate species, the data are insufficient for determining the MOA among mollusks and arthropods. For the tested vertebrate species, data were consistent with the estrogen agonist MOA among fish and mammals, whereas data were insufficient to make conclusions about the MOA among reptiles and amphibians. A relationship between species relatedness and the estrogen agonist MOA was found among fish and mammals. Thus, the cross-species MOA approach holds promise for applying MOA information in integrated risk assessment, and predicting the MOA for untested species for toxic agents with an established MOA among related species.